General

Guideline Title

Canagliflozin, dapagliflozin and empagliflozin as monotherapies for treating type 2 diabetes.

Bibliographic Source(s)

National Institute for Health and Care Excellence (NICE). Canagliflozin, dapagliflozin and empagliflozin as monotherapies for treating type 2 diabetes. London (UK): National Institute for Health and Care Excellence (NICE); 2016 May 25. 47 p. (Technology appraisal guidance; no. 390).

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Regulatory Alert

FDA Warning/Regulatory Alert

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- May 16, 2017 – Canagliflozin (Invokana, Invokamet) : Based on new data from two large clinical trials, the FDA has concluded that the type 2 diabetes medicine canagliflozin (Invokana, Invokamet, Invokamet XR) causes an increased risk of leg and foot amputations. FDA is requiring new warnings, including the most prominent Boxed Warning, to be added to the canagliflozin drug labels to describe this risk.

Recommendations

Major Recommendations

Canagliflozin, dapagliflozin and empagliflozin as monotherapies are recommended as options for treating type 2 diabetes in adults for whom metformin is contraindicated or not tolerated and when diet and exercise alone do not provide adequate glycaemic control, only if:

- A dipeptidyl peptidase-4 (DPP-4) inhibitor would otherwise be prescribed and
- A sulfonylurea or pioglitazone is not appropriate

Adults whose treatment with canagliflozin, dapagliflozin or empagliflozin as monotherapy is not recommended in this National Institute for Health and Care Excellence (NICE) guidance, but was started within the National Health Services (NHS) before this guidance was published, should be able to continue treatment until they and their NHS clinician consider it appropriate to stop.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Type 2 diabetes

Guideline Category

Assessment of Therapeutic Effectiveness

Treatment

Clinical Specialty

Endocrinology

Family Practice

Internal Medicine

Intended Users

Advanced Practice Nurses

Physician Assistants

Physicians

Guideline Objective(s)

To assess the clinical effectiveness and cost-effectiveness of canagliflozin, dapagliflozin and empagliflozin as monotherapies for treating type 2 diabetes

Target Population

Adults with type 2 diabetes

Interventions and Practices Considered

1. Canagliflozin monotherapy
2. Dapagliflozin monotherapy
3. Empagliflozin monotherapy

Major Outcomes Considered

- Clinical effectiveness
  - Mortality
  - Complications of diabetes
  - Glycosylated haemoglobin (HbA1c)/glycaemic control
  - Body mass index
  - Frequency and severity of hypoglycaemia
  - Changes in cardiovascular risk factors
  - Adverse effects of treatment
  - Health-related quality of life
- Cost-effectiveness

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Care Excellence (NICE) commissioned an independent academic centre to perform an assessment of the technology considered in this appraisal and prepare an Assessment Report. The Assessment Report for this technology appraisal was prepared by Warwick Evidence (see the "Availability of Companion Documents" field).

Clinical Effectiveness

Inclusion Criteria

Types of Studies

The Assessment Group (AG) included randomised controlled trials (RCTs) with a minimum duration of 24 weeks. Observational studies were included to assess safety data.

Types of Participants

The AG included trials in people with type 2 diabetes on diet and exercise therapy only or in people on monotherapy with a glucose-lowering agent after a washout period. The target group was patients with type 2 diabetes unable to take metformin, but this distinction was not made in the trials.

A search was carried out for studies comparing people who can and cannot tolerate metformin, looking for any differences in factors that might affect the modelling, such as weight, blood pressure, cholesterol. Nothing significant was found.

Types of Interventions

Only trials of monotherapy were included.

To be included, trials had to investigate canagliflozin (100 mg or 300 mg), dapagliflozin (10 mg) or empagliflozin (10 mg or 25 mg). Eligible comparators were repaglinide, gliclazide as representative of the sulfonylureas, pioglitazone, dipeptidyl peptidase-4 (DPP-4) inhibitors (the gliptins), or placebo.

The three flozins were also compared with each other. As there were no head to head trials of the flozins, data from a network meta-analysis were required.

Types of Outcomes

Studies were eligible if they investigated at least one of the following outcomes:

- Mortality
- Complications of diabetes, including cardiovascular, renal and eye
- Glycosylated haemoglobin (HbA1c)/glycaemic control
- Body mass index
- Frequency and severity of hypoglycaemia
- Changes in cardiovascular risk factors
- Adverse effects of treatment, including urinary tract infections, genital infections and malignancies
- Health-related quality of life

Search Strategy

Searches were run in Ovid Medline, EMBASE and Web of Science from the inception of the databases until February 2015. Thereafter weekly auto-alerts were run in PubMed in process and EMBASE until September 2015 to check for newly emerging studies. The searches were not restricted by language or publication type. The full search strategy is shown in Appendix 1 of the Assessment Report.

Selection of Studies

Two reviewers independently checked titles and abstracts of the search results against the inclusion criteria. Studies were retrieved in full if they appeared to fulfil the inclusion criteria or when eligibility could not be determined from the search results alone.

Results

A total of 1039 of records were identified through database searching. After duplicates were removed, 628 records were screened. Seven studies were included in the final analysis. See Appendix 1 of the Assessment Report for the PRISMA flow diagram of clinical effectiveness studies.

Refer to the "Methods" section in Chapter 3 of the Assessment Report for selection methods for the network meta-analysis.

Cost-effectiveness

AG Cost-effectiveness Literature Review

Only one paper was identified that addressed the cost-effectiveness of flozin monotherapy in the patient group under consideration.

Number of Source Documents

Clinical Effectiveness

- Seven studies were included in the final analysis (2 each for canagliflozin and empagliflozin and 3 for dapagliflozin).
- Ten additional studies were also included for network meta-analysis.

Cost-effectiveness

- One paper was identified.
- The manufacturers of canagliflozin, dapagliflozin and empagliflozin, and the Assessment Group (AG) submitted economic models.

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus

Rating Scheme for the Strength of the Evidence

Not applicable

Methods Used to Analyze the Evidence

Meta-Analysis

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Care Excellence (NICE) commissioned an independent academic centre to perform an assessment of the technology considered in this appraisal and prepare an Assessment Report. The Assessment Report for this technology appraisal was prepared by Warwick Evidence (see the "Availability of Companion Documents" field).

Clinical Effectiveness

Assessment of Study Quality

The quality of the randomised controlled trials (RCTs) was assessed using the Cochrane risk of bias tool, which included the following items (rated as adequate, unclear, not reported, or inadequate):

- Method of randomisation
- Allocation concealment
- Blinding of participants and personnel
- Blinding of outcome assessment
- Incomplete outcome data (>20% drop-out regarded as inadequate)
- Intention-to-treat analysis
- Selective reporting
- Similarity at baseline
- Other (e.g., power analysis)

Overall quality was expressed in terms of proportion of items rated as 'adequate'.

Quality was assessed by one reviewer and checked by a second reviewer.

Data Extraction

Data were extracted using a pre-designed data extraction table, with one reviewer extracting and another reviewer checking the data.

Results were expressed as means and standard deviations. Standard errors and confidence intervals were converted to standard deviations using the equations provided in the Cochrane handbook. Results for lipids were expressed as mmol/L. Cholesterol values expressed in mg/dL were converted to mmol/L by dividing by 38.67 and lipid values expressed in mg/dL were converted to mmol/L by dividing by 88.57.

Data Summary

Data were summarised using text and tables.

The following subgroup analyses were considered:

- Body mass index (BMI) <25, 25-29, 30 and over
- Baseline glycosylated haemoglobin (HbA1c)

Network Meta-analysis of Sodium-Glucose Co-transporter-2 (SGLT2) Inhibitors and Comparators in Monotherapy

The aim of the network meta-analysis (NMA) was not only to compare canagliflozin, empagliflozin and dapagliflozin, but also to assess their effects relative to active comparators.

Data Synthesis and Model Implementation

The Assessment Group (AG) used a Bayesian network meta-analysis method to analyse all the data, preserving randomized treatment effects within trials and accounting for correlation between comparisons with three-arms or four-arms using the freely available software, WinBUGS 1.4.3. The statistical heterogeneity in treatment effect estimates was estimated using between study variance (i.e., square root of the standard deviation of underlying effects across trials) with 95% credible interval (CrI). To estimate inconsistency in the networks of evidence, the AG calculated the difference between indirect and direct estimates whenever indirect estimates could be constructed with a single common

comparator. Inconsistency was defined as disagreement between direct and indirect evidence with a 95% CrI excluding 0 for mean difference (MD). The model convergence was assessed using trace plots and the Brooks-Gelman-Rubin statistic. The analysis was undertaken using two Markov chains, which was run simultaneously. The model was found to be converging adequately after 20,000 samples for both chains. The AG ran the model further using 70,000 samples and the results presented in the paper are based on these samples as the AG discarded the first 20,000 samples.

Both the fixed and random effect models were used. The Bayesian Deviation Information Criterion (DIC) was used to compare the two models to see which was appropriate to compare treatment effects. The DIC measures the fit of the model while penalizing it for the number of effective parameters. The model with the lowest DIC value was considered as the most appropriate NMA model. Based on DIC values obtained from the two models and also because of small number of studies available for the NMA, a fixed effect model was chosen. Due to small number of studies, it would have been difficult to estimate between studies variance if a random effect model was implemented.

All results are reported as posterior medians of MDs with corresponding 95% CrIs. CrIs are the Bayesian equivalent of classic confidence intervals. A 95% CrI can be interpreted as there being a 95% probability that the parameter takes a value in the specified range. Drugs were not ranked, but were considered in terms of effect sizes and uncertainties.

See Chapters 2 and 3 of the Assessment Report for additional information on clinical effectiveness and network meta-analysis, respectively.

Cost-effectiveness

The manufacturers of canagliflozin, dapagliflozin and empagliflozin, and the AG submitted economic models.

Company Submissions

All the submissions contain modelling exercises with long term time horizons of around 40 years, which for the majority of patients will be a lifetime horizon. They all undertake a cost utility analysis using the appropriate perspectives of the National Health Service (NHS) and Personal Social Services (PSS) for costs and the patient for benefits, and discount costs and benefits at 3.5%.

Boehringer Ingelheim designed a front end to the U.K. Prospective Diabetes Study Outcomes Model 1 (UKPDS OM1) model. The Boehringer Ingelheim submission has a great deal in common with the modelling of recent NICE clinical guidelines for type 2 diabetes mellitus (T2DM) and the AG modelling for the current assessment, both of which design a front end to the UKPDS OM1.

Astrazeneca uses the CARDIFF diabetes model (CDM) which uses many of the UKPDS68 equations and so has much in common with the UKPDS OM1 model, but updates the calculation of the probabilities of having an event to use the UKPDS82 which is the basis of the OM2.

Janssen differs from Astrazeneca and Boehringer Ingelheim in using the Economic and Health Outcomes Model for Type 2 Diabetes Mellitus (ECHO-T2DM) model. Its base case has assumptions which differ quite noticeably from those of the other two submissions.

See Chapter 5 of the Assessment Report for details on manufacturers' models.

Assessment Group Economic Modelling

The Model

The protocol specified that either the UKPDS OM1 or the UKPDS OM2 would be used by the AG. For some of its outputs the OM1 is quite different from the OM2 in its predictions. But the OM2 was not made available to the AG in time for the assessment and so as specified in the protocol the OM1 has been used.

The OM1 was used for the modelling that underlies the NICE clinical guideline (CG) for diabetes (see the NGC summary of the NICE guideline Type 2 diabetes in adults: management). During its development the Guideline Development Group (GDG) reviewed in detail ten T2DM cost-effectiveness models. These included the JADE and CORE models, but not the ECHO-T2DM model. Based upon validation and consistency with the NICE reference case the GDG very much preferred the OM1, in no small part due to it being based upon a single RCT rather than drawing a range of modelling inputs from disparate sources.

The AG has developed a front and back end to the OM1. Briefly, for each patient and treatment strategy that is simulated the AG front end models the patient's progression from monotherapy through the various treatment intensifications over a 40 year time horizon in annual cycles. This in turn introduces the patient's evolutions of HbA1c, systolic blood pressure (SBP), total cholesterol:high density lipoprotein (TC:HDL), BMI, hypoglycaemia event rates, adverse events and treatment costs. The evolutions of the patient's HbA1c, SBP and TC:HDL are then fed into the OM1 which models the complications of diabetes and patient lifespan, and outputs the costs and quality of life impacts of living with diabetes and the patient's survival curve. The AG back end takes the OM1 survival curve and uses this to condition the evolutions of the patient's BMI,

hypoglycaemia event rates, adverse events and treatment costs. The cost and quality of life impacts of these are then summed with the cost and quality of life impacts outputted by the OM1.

In slightly more detail, patients start on monotherapy but intensify their treatment if their HbA1c is modelled as breaching the 7.5% threshold. Intensifications typically add another treatment to a patient's existing treatment(s). This permits treatment sequences to be modelled, starting with monotherapy but with subsequent treatment intensifications, these intensifications eventually leading to first basal insulin and then basal-bolus insulin. Each treatment within a sequence is associated with treatment costs, weight changes, hypoglycaemic events and adverse events. The AG modelling also permits treatments to be associated with a discontinuation rate in their first year, with patients who discontinue being assumed to switch to another treatment at the same line of therapy.

See Chapter 5 of the Assessment Report for more information on model structure and cost-effectiveness analysis.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Considerations

Technology appraisal recommendations are based on a review of clinical and economic evidence.

Technology Appraisal Process

The National Institute for Health and Care Excellence (NICE) invites 'consultee' and 'commentator' organisations to take part in the appraisal process. Consultee organisations include national groups representing patients and carers, the bodies representing health professionals, and the manufacturers of the technology under review. Consultees are invited to submit evidence during the appraisal and to comment on the appraisal documents.

Commentator organisations include manufacturers of the products with which the technology is being compared, the National Health Service (NHS) Quality Improvement Scotland and research groups working in the area. They can comment on the evidence and other documents but are not asked to submit evidence themselves.

NICE then commissions an independent academic centre to review published evidence on the technology and prepare an 'Assessment Report. Consultees and commentators are invited to comment on the report. The assessment report and the comments on it are then drawn together in a document called the evaluation report.

An independent Appraisal Committee then considers the evaluation report. It holds a meeting where it hears direct, spoken evidence from nominated clinical experts, patients and carers. The Committee uses all the evidence to make its first recommendations, in a document called the Appraisal Consultation Document (ACD). NICE sends all the consultees and commentators a copy of this document and posts it on the NICE Web site. Further comments are invited from everyone taking part.

When the Committee meets again it considers any comments submitted on the ACD; then it prepares its final recommendations in a document called the Final Appraisal Determination (FAD). This is submitted to NICE for approval.

Consultees have a chance to appeal against the final recommendations in the FAD. If there are no appeals, the final recommendations become the basis of the guidance that NICE issues.

Who Is on the Appraisal Committee?

NICE technology appraisal recommendations are prepared by an independent committee. This includes health professionals working in the NHS and people who are familiar with the issues affecting patients and carers. Although the Appraisal Committee seeks the views of organisations representing health professionals, patients, carers, manufacturers and government, its advice is independent of any vested interests.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

Summary of Appraisal Committee's Key Conclusions

Availability and Nature of Evidence

The Assessment Group (AG) and all the companies used existing economic models for diabetes to consider the cost effectiveness of sodium-glucose co-transporter-2 (SGLT-2) inhibitor monotherapy.

Uncertainties Around and Plausibility of Assumptions and Inputs in the Economic Model

The committee noted that the manufacturer's model had highly favourable incremental cost-effectiveness ratios (ICERs) of £4,400 to £7,900 per quality-adjusted life year (QALY) gained for canagliflozin 100 mg or 300 mg compared with sulfonylureas, whereas ICERs in the other models were substantially higher. The committee concluded there was uncertainty about the reason for the favourable cost-effectiveness results for canagliflozin compared with a sulfonylurea in the manufacturer's model, but that the increased costs arising from retaining oral treatments (a committee preferred assumption) was likely to be an important contributing factor.

The committee noted that the small QALY differences between treatments made the ICERs unstable.

Incorporation of Health-related Quality-of-Life Benefits and Utility Values. Have Any Potential Significant and Substantial Health-related Benefits Been Identified That Were Not Included in the Economic Model, and How Have They Been Considered?

The committee noted that there were generally very small QALY differences between the various treatments. It also noted that the AG had presented a number of scenarios varying the impact of body mass index (BMI) on quality of life. Overall the committee agreed that weight loss does affect quality of life and that the evidence had shown that SGLT-2 inhibitors do have a significant effect on weight loss. It noted that National Institute for Health and Care Excellence's (NICE's) guideline on diabetes (see the NGC summary of the NICE guideline Type 2 diabetes in adults: management) used the same assumption for the duration of weight gains and losses as that used in scenario BMI-2. It concluded that BMI-2 was the most plausible scenario, but noted that the small QALY differences between treatments made the ICERs unstable.

Are There Specific Groups of People for Whom the Technology Is Particularly Cost Effective?

No specific committee consideration.

What Are the Key Drivers of Cost-effectiveness?

The key driver of cost-effectiveness was the BMI scenario chosen. The committee concluded that BMI-2 was the most plausible scenario, but noted that the small QALY differences between treatments made the ICERs unstable.

Most Likely Cost-effectiveness Estimate (Given as an ICER)

When the SGLT-2 inhibitors were compared with each other, the committee agreed that the clinical and cost evidence did not support any differences between them.

When compared with pioglitazone, ICERs for all the SGLT-2 inhibitors were more than £52,400 per QALY gained.

When compared with sulfonylureas, ICERs for the SGLT-2 inhibitors were all more than £71,000 per QALY gained.

When compared with DPP-4 inhibitors, the ICERs ranged from £3,600 to £29,300 per QALY gained.

Method of Guideline Validation

External Peer Review

Description of Method of Guideline Validation

Consultee organisations from the following groups were invited to comment on the draft scope, Assessment Report and the Appraisal Consultation Document (ACD) and were provided with the opportunity to appeal against the Final Appraisal Determination (FAD).

- Manufacturer/sponsors
- Professional/specialist and patient/carer groups

- Commentator organisations (without the right of appeal)

In addition, individuals selected from clinical expert and patient advocate nominations from the professional/specialist and patient/carer groups were also invited to comment on the ACD.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

The Appraisal Committee considered clinical and cost-effectiveness evidence submitted by the manufacturers of canagliflozin, dapagliflozin and empagliflozin and a review of this submission by the Assessment Group (AG). The main clinical effectiveness evidence came from randomised controlled trials. For cost-effectiveness, the Appraisal Committee considered economic models submitted by the manufacturers and the AG.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Canagliflozin, dapagliflozin and empagliflozin are all selective sodium-glucose cotransporter 2 (SGLT-2) inhibitors, which block the reabsorption of glucose in the kidneys and promote excretion of excess glucose in the urine. Through this mechanism these drugs may help control glycaemia independently of insulin pathways.

Potential Harms

The summaries of product characteristics list the following adverse reactions for:

- Canagliflozin: balanitis, constipation, dyslipidaemia, haematocrit increase, nausea, polyuria, thirst, urinary tract infection and vulvovaginal candidiasis
- Dapagliflozin: back pain, balanitis, creatinine renal clearance decrease, dizziness, dysuria, dyslipidaemia, elevated haematocrit, polyuria, urinary tract infection and vulvovaginitis. Dapagliflozin is not recommended for people with moderate to severe renal impairment (people with a creatinine clearance rate of less than 60 ml/min or an estimated glomerular filtration rate [eGFR] of less than 60 ml/min/1.73m^2).
- Empagliflozin: balanitis, increased urination, pruritus, urinary tract infection, vaginal moniliasis and vulvovaginitis

For full details of adverse reactions and contraindications, see the summaries of product characteristics.

Contraindications

Contraindications

For full details of adverse reactions and contraindications, see the summaries of product characteristics.

Qualifying Statements

Qualifying Statements

- The recommendations in this guidance represent the view of the National Institute for Health and Care Excellence (NICE), arrived at after careful consideration of the evidence available. When exercising their judgement, health professionals are expected to take this guidance fully

into account, alongside the individual needs, preferences and values of their patients. The application of the recommendations in this guidance are at the discretion of health professionals and their individual patients and do not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

- Commissioners and/or providers have a responsibility to provide the funding required to enable the guidance to be applied when individual health professionals and their patients wish to use it, in accordance with the National Health Service (NHS) Constitution. They should do so in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities.

Implementation of the Guideline

Description of Implementation Strategy

- Section 7(6) of the National Institute for Health and Care Excellence (NICE) (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 requires clinical commissioning groups, National Health Services (NHS) England and, with respect to their public health functions, local authorities to comply with the recommendations in this appraisal within 3 months of its date of publication.
- The Welsh Assembly Minister for Health and Social Services has issued directions to the NHS in Wales on implementing NICE technology appraisal guidance. When a NICE technology appraisal recommends the use of a drug or treatment, or other technology, the NHS in Wales must usually provide funding and resources for it within 3 months of the guidance being published.
- When NICE recommends a treatment 'as an option', the NHS must make sure it is available within the period set out in the paragraphs above. This means that, if a person has type 2 diabetes and the doctor responsible for their care thinks that canagliflozin, dapagliflozin or empagliflozin as monotherapy is the right treatment, it should be available for use, in line with NICE's recommendations.

Implementation Tools

Foreign Language Translations

Mobile Device Resources

Patient Resources

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

National Institute for Health and Care Excellence (NICE). Canagliflozin, dapagliflozin and empagliflozin as monotherapies for treating type 2 diabetes. London (UK): National Institute for Health and Care Excellence (NICE); 2016 May 25. 47 p. (Technology appraisal guidance; no. 390).

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2016 May 25

Guideline Developer(s)

National Institute for Health and Care Excellence (NICE) - National Government Agency [Non-U.S.]

Source(s) of Funding

National Institute for Health and Care Excellence (NICE)

Guideline Committee

Appraisal Committee

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Financial Disclosures/Conflicts of Interest

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the National Institute for Health and Care Excellence (NICE) Web site. Also available for download in ePub and eBook formats from the NICE Web site.

Availability of Companion Documents

The following are available:

- Johnston R, Uthman O, Cummins E, Clar C, Royle P, Colquitt J, Tan B, Clegg A, Shantikumar S, Court R, O'Hare P, McGrane D, Holt T, Waugh N. Canagliflozin, dapagliflozin and empagliflozin monotherapy for treating type 2 diabetes: systematic review and economic evaluation. Assessment report. Coventry (UK): Warwick Evidence; 2015 Oct 4. 304 p. Available from the National Institute for Health and Care Excellence (NICE) Web site.
- Canagliflozin, dapagliflozin and empagliflozin as monotherapies for treating type 2 diabetes. Resource impact report. London (UK): National Institute for Health and Care Excellence (NICE); 2016 May. 3 p. (Technology appraisal guidance; no. 390). Available from the NICE Web site.

Patient Resources

The following is available:

- Canagliflozin, dapagliflozin and empagliflozin as monotherapies for treating type 2 diabetes. Information for the public. London (UK): National Institute for Health and Care Excellence (NICE); 2016 May. 3 p. (Technology appraisal guidance; no. 390). Available in English and Welsh from the National Institute for Health and Care Excellence (NICE) Web site. Also available for download in ePub and eBook formats from the NICE Web site.

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NGC Status

This NGC summary was completed by ECRI Institute on October 4, 2016. This summary was updated by ECRI Institute on July 11, 2017 following the U.S. Food and Drug Administration advisory on Canagliflozin (Invokana, Invokamet).

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